



## UNITED STATES DEPARTMENT OF COMMERCE

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EXAMINER

DERRIDA, J.

WILFRED G. DIAZ  
GENZYME CORP.  
ONE BENJAMIN DR.  
CAMBRIDGE, MA 02142

ART UNIT	PAPER NUMBER
	9

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This is a communication from the examiner in charge of your application.  
COMMISSIONER OF PATENTS AND TRADEMARKS

 This application has been examined Responsive to communication filed on 9/8/93  This action is made final.

A shortened statutory period for response to this action is set to expire three (3) month(s), — days from the date of this letter.  
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

## Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1.  Notice of References Cited by Examiner, PTO-892.
2.  Notice re Patent Drawing, PTO-948.
3.  Notice of Art Cited by Applicant, PTO-1449.
4.  Notice of Informal Patent Application, Form PTO-152.
5.  Information on How to Effect Drawing Changes, PTO-1474.
6.

## Part II SUMMARY OF ACTION

1.  Claims 1, 2, 4-9 and 11 are pending in the application.

Of the above, claims \_\_\_\_\_ are withdrawn from consideration.

2.  Claims 3 have been cancelled.

3.  Claims \_\_\_\_\_ are allowed.

4.  Claims 1, 2, 4-9 and 11 are rejected.

5.  Claims \_\_\_\_\_ are objected to.

6.  Claims \_\_\_\_\_ are subject to restriction or election requirement.

7.  This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.

8.  Formal drawings are required in response to this Office action.

9.  The corrected or substitute drawings have been received on \_\_\_\_\_. Under 37 C.F.R. 1.84 these drawings are  acceptable.  not acceptable (see explanation or Notice re Patent Drawing, PTO-948).

10.  The proposed additional or substitute sheet(s) of drawings, filed on \_\_\_\_\_ has (have) been  approved by the examiner.  disapproved by the examiner (see explanation).

11.  The proposed drawing correction, filed on \_\_\_\_\_, has been  approved.  disapproved (see explanation).

12.  Acknowledgment is made of the claim for priority under U.S.C. 119. The certified copy has  been received  not been received  been filed in parent application, serial no. \_\_\_\_\_; filed on \_\_\_\_\_.

13.  Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.

14.  Other

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EXAMINER'S ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1, 2, 5-9 and 11, newly amended, remain rejected under 35 U.S.C. 112, first paragraph, as the disclosure is enabling only for claims limited to a DNA sequence comprising a whey acidic protein promoter, as applied in the last Office action.

Applicants' arguments in the Amendment and the Gordon Declarations, all filed on September 8, 1993, have been carefully considered but are not deemed persuasive. Although Applicants argue that "at the time the claimed invention was made, it was reasonable to expect milk proteins to share similar regulatory mechanisms and regulatory sequences" (page 4 of the Amendment), they have not submitted any objective evidence (e.g., published reports on the comparisons of milk protein regulatory sequences, etc.) to support their statement. Thus, Applicants' assertion represents nothing more than speculation. The Gordon Declaration similarly states that "milk proteins coordinately expressed in lactating mammary epithelia were presumed to share similar regulatory mechanisms for expression" (emphasis added, page 4 of the Declaration). Again, such statement represents no more than an opinion which is not supported by any data or objective evidence. Furthermore, the specification provides little or no guidance on the isolation and identification of regulatory sequences of other milk serum proteins. It was well known in the art that "experiments in genetic engineering produce, at best, unpredictable results" (*Ex parte Forman*, 230 USPQ 546 (BPAI 1986)). It is also noted that the unpredictability of a particular art area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claim. See *Ex parte Singh*, 17 USPQ2d 1714 (BPAI 1991). Accordingly, the disclosure remains enabling only for claims limited to a DNA sequence comprising a whey acidic protein promoter.

Claims 1, 2, 4 and 6-9, newly amended, remain rejected under 35 U.S.C. 103 as being unpatentable over Andres et al., as applied in the last Office action.

Claims 5 and 11, newly amended, remain rejected under 35 U.S.C. 103 as being unpatentable over Andres et al., as applied to claims 1-4 and 6-9 above, and further in view of Pennica et al. or Chisari et al., as applied in the last Office action.

Applicants' arguments on pages 5-6 of the Amendment filed on September 8, 1993 have been carefully considered but are not deemed persuasive. Firstly, it should be noted that the claims are not specifically directed to therapeutically active proteins (terms used in Applicants' arguments, see page 5 of the Amendment), nor do the claims specifically exclude H-ras or other oncogene products. Thus, the claims are directed to a DNA construct comprising genes coding for all proteins. Thus, the only difference between the DNA construct of the claimed invention and the construct disclosed by Andres et al. is the presence of a signal peptide sequence. It is also noted that at the time the claimed invention was made, signal peptide sequences (of milk proteins as well as of other proteins) enabling the secretion of proteins were well known. Thus, if one of ordinary skill in the art so desired to have secretion of the recombinant proteins into milk, one of ordinary skill would have obviously included a signal peptide sequence into the DNA construct for the expected benefit of obtaining secretion of the recombinant proteins (H-ras and other proteins). Applicants were correct to point out that the teachings of Andres et al. did not suggest modifying their H-ras DNA construct by including a signal peptide sequence because there was no motivation to produce a secreted form of the H-ras protein (page 5 of the Amendment). However, if one were to produce other recombinant proteins using a similar DNA construct and desired to have secretion of the recombinant proteins into milk, it would certainly have been within the ordinary skill of the art at the time the claimed invention as made

to include one of the many well-known signal peptide sequences in the DNA construct. Accordingly, in the absence of unexpected results, the rejections are maintained.

Claims 1, 2, 4-9 and 11, newly amended, remain rejected under 35 U.S.C. 103 as being unpatentable over Campbell et al., when taken with either Pennica et al. or Chisari et al., and further in view of any one of Palmiter et al., Ross et al. or Stewart et al., as applied in the last Office action.

Applicants' arguments on pages 6-9 of the Amendment filed on September 8, 1993 have been carefully considered but are not deemed persuasive. Applicants attempt to point out differences between their claimed invention and the teachings of each of the cited references. They argue that Pennica et al. does not "bridge the gap between Campbell et al. and the claimed DNA constructs" or "supply the necessary suggestion to modify Campbell et al." and that "suggestion is neither explicit in, nor fairly inferred" from Chisari et al.. They additionally assert that Palmiter et al. does not "discuss or infer the production of recombinant proteins in milk of transgenic animals" and that Ross et al. and Stewart et al. do not "teach or suggest that Campbell et al. be modified". Finally, Applicants assert that "the claimed DNA construct serves a purpose, and has properties, that are not disclosed or suggested in the prior art" (page 9 of the Amendment). It is apparent that Applicants are arguing each of the cited references individually and separately. It is noted that the test for combining references is not what the individual references themselves suggest but rather what the combination of disclosures taken as a whole would have suggested to one of ordinary skill in the art. *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). Furthermore, for the purpose of combining references, those references need not explicitly suggest combining teachings, much less specific references. *In re Nilssen*, 7 USPQ2d 1500 (CAFC 1988). It is maintained that the teachings of the cited references, when taken as a whole, would have reasonably suggested to one of ordinary skill

in the art at the time the claimed invention was made a DNA construct identical or similar to that claimed by Applicants. Accordingly, in the absence of unexpected results, the rejections are maintained.

No claim is allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). The practice of automatically extending the shortened statutory period an additional month upon the filing of a timely first response to a final rejection has been discontinued by the Office. See 1021 TMOG 35.

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 CFR 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Any inquiry concerning this communication should be directed to Jasemine C. Chambers, Ph. D., at telephone number (703) 308-2035.

*Jasemine C. Chambers*  
JASEMINE C. CHAMBERS  
PRIMARY EXAMINER  
GROUP 1800